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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,767	01/10/2002	Wolf B. Frommer	056100-5039-US	4393

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EXAMINER	
IBRAHIM, MEDINA AHMED	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 07/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,767	FROMMER ET AL.	
	Examiner	Art Unit	
	Medina A. Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,25,26,28-38,40-42,44-48 and 56-65* is/are pending in the application.

4a) Of the above claim(s) *35,36,40 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23, 25-26, 28-34, 37-38, 41-42, 45-48 and 56-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's response filed 04/18/05 in reply to the Office action of 11/16/04 has been entered. Claims 24, 27, 39, 43, and 49-55 have been cancelled. Claims 57-65 have been added. Claims 23, 25, 26, 28-34, 37-38, 41-42, 45-48 and 56 have been amended. Therefore, claims 23, 25-26, 28-38, 40-42, 44-48, and 56-65 are pending. Claims 35-36, 40, and 44 have been withdrawn from consideration.

All previous objections and rejections not set forth below have been withdrawn. This Office action contains NEW GROUNDS OF REJECTIONS not necessitated by Applicant's amendments. Therefore, this action is non-final. The delay in applying these grounds of rejection is regretted.

Claims 23, 25-26, 28-34, 37-38, 41-42, 45-48 and 56-65 are under consideration.

Claim Objections

At claim 28, "sequence" in line 1 should be deleted for proper dependency.

Claim Rejections - 35 USC § 112

Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 is indefinite for depending upon cancelled claim 24. In the interest of compact prosecution, the claim is considered to depend from claim 23.

Claim Rejections - 35 USC § 112

Claims 23, 25-26, 28-34, 37-38, 41-42, 45-48 and 56-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid sequence encoding SEQ ID NO: 8, the nucleic acid of SEQ ID NO: 1, host cells/plants/parts/seed comprising said nucleic acid sequence, and a method for transforming a plant/cell with said nucleic acid sequence, does not reasonably provide enablement for a nucleic acid sequence encoding any plant or animal nuclear base transporter, fragments of 10, 50 or 200 nucleotides thereof and a nucleic acid sequence that hybridizes to a nucleic acid sequence that encodes SEQ ID NO: 8 or 9 under the conditions as recited in claim 23, a nucleic acid that codes for nuclear base transporter having at least 40% identity to SEQ ID NO: 8 or 9 host cells/plants/parts comprising said nucleic acid sequence, and a method for using said nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is repeated for the reasons of record as set forth in the last Office action of 11/16/04. Applicant's arguments filed 04/18/05 have been considered but are not deemed persuasive.

Applicant argues that the instant specification discloses at least eight plant nuclear base transporter nucleic acids that meet the limitations of claim 23. Applicant refers to the nucleic acid of SEQ ID NO: 1 and the sequences of SEQ ID NO: 2, 3, 4, 5, 6, 7, or 10 identified by homology. Applicant asserts that these homologous sequences

would predictably have properties similar to SEQ ID NO: 1 (response, paragraph bridging pages 21 and 22).

This is not found persuasive because the scope of the nucleic acids of the claimed invention is not supported by enabling disclosure. The scope of the nucleic acids of claim 23 encompasses any nucleic acid from any plant species or animal source encoding a nuclear base transporter including those that hybridizes to a nucleic acid encoding SEQ ID NO: 8 or 9, and the coding sequence of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7 and 10. The specification provides guidance for a single nucleic acid, SEQ ID NO: 1, from a single plant species of Arabidopsis. The other sequences, SEQ ID NO: 2, 3, 4, 5,6, 7 and 10 listed in the claims, are also from Arabidopsis, and even if these sequences identified by homology have a nuclear base transport activity, Applicant has not taught how to use them in transgenic plants because they have no known function. Applicant discloses no property that relates these homologous sequences to nuclear base transport activity, and no evidence to support the conclusion that sequences identified by homology would predictably have a functional property similar to SEQ ID NO: 1.

Gillissen et al (The plant Cell (2000), vol. 12, pp. 291-300) teaches about transporters of adenine, cytosine, and purine and derivates in plants. Gillissen et al states that while nucleic acid base and nucleoside uptake in plants are known, respective transport genes have not been isolated (see page 291, column 1). In addition, Applicant has not provided guidance for a single nucleic acid encoding animal nuclear base transporter or how to use it in a transgenic plant. Therefore, to claim a

nucleic acid encoding any plant or animal nuclear transporter without specific guidance for how to identify and use them is an invitation to experiment requiring undue experimentation.

Applicant also argues against the citations of Chen et al and Newman et al. Applicant asserts that Chen et al, who teach a putative amino acid transporter from a plant failed to complement the functional activity of a yeast amino acid transporter mutant, and Newman et al are not relevant to the enablement instant claims (response, 2nd and 3rd full paragraphs of page 22).

This is not persuasive. The examiner maintains that Chen et al reference is relevant because it provides the unpredictability inherent in identifying a plant transporter protein encoding nucleic acid by functional complementation in yeast. Claims 23, 25 are drawn to nucleic acids encoding a plant nuclear transporter obtained by functional complementation. Newman et al was relied upon because it provides evidence that every 10, 50 and 200 nucleotides of SEQ ID NO: 1 (or other sequences listed in claims 26 and 45-46) is not enabled or has function. Newman et al (Accession no. H76984, disclosed in the last Office action) teach a nucleic acid sequence with more than 160 contiguous bases of SEQ ID NO: 1 having no known base transport activity. Note, the nucleic acid of claims 26 and 45-46 are not required to be contiguous. Therefore, Chen et al and Newman are relevant to the rejected claims. Therefore, Chen et al and Newman are considered relevant to the rejected claims.

Applicant further argues that multiple site directed mutagenesis in a single gene is routine, and that a considerable amount of experimentation is permissible, if it is

merely routine or if the specification provides guidance regarding the direction in which experimentation should proceed. Applicant asserts that it is not necessary that Applicant teach specific positions that can be modified when Applicant discloses assays to select and identify active mutants.

This is not persuasive because Applicant points to no specific methods that are known or disclosed in the instant specification which provides nucleic acids of the claim 23, parts (a), (c), (d), claims 26 and 45-46. Applicant cites no reference or scientific publication that teaches multiple site mutageneses in a specific gene that retains the original gene function. Applicant points to no suitable yeast systems for the selection and identification of the nucleic acids as broadly claimed. MPEP 2164 .03 states (t)he more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). In this application, very little is known about plant nuclear base transport system and nuclear transport protein encoding genes as evidenced by Applicant's own specification.

Given that the specification teaches only a single sequence, SEQ ID NO: 1, from a single plant species, Arabidopsis; the limited information in the prior art regarding isolated plant nuclear transport genes and their function; and given that no guidance has been provided for regions in the full-length sequence of SEQ ID NO: 1 that would

tolerate modifications or the functional domains essential for base transport activity; the claimed invention cannot be practiced throughout the broad scope, without undue experimentation as stated in the last Office action.

See Genentech Inc v. Novo Nordisk A/S (42 USPQ2d 1001 at p. 1005). The CAFC stated, "(P)atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable....While every aspect of generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention....[w]hen there is no disclosure of any specific starting material or conditions under which a process can be carried out, undue experimentation is required...."

Written Description

Claims 23, 25-26, 28-34, 37-38, 41-42, 45-48 and 56-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reasons of record as set forth in the last Office action of 11/16/04. Applicant's arguments filed 04/18/05 have been considered but are not deemed persuasive.

Applicant argues that the instant specification describes the at least eight different plant nuclear base transporter nucleic acids including SEQ ID NO: 1 identified by functional complementation in yeast and sequences identified by homology analysis

which would predictably possess property similar to SEQ ID NO: 1, are sufficient to provide adequate written description for the genus claimed.

This is not found persuasive because the disclosure of eight nucleic acids from a single plant species is insufficient to provide adequate written description for the genus encompassing all nucleic acids encoding any plant or animal nuclear base transporter, all nucleic acids that hybridize to a nucleic acid sequence that encodes SEQ ID NO: 8 or 9 under the conditions as recited in claim 23, all nucleic acids encoding a nuclear base transporter having at least 40% identity to SEQ ID NO: 8 or 9, and fragments of 10, 50 or 200 nucleotides of SEQ ID NO: 1, 2, 3 , 4, 5, 6, 7 or 10. A substantial variation in structures and function is expected among the nucleic acids of the genus. Applicant has neither described a representative number of nucleic acids falling within the scope of the genus nor disclosed structural features common to members of the genus, which features constitute a substantial portion of the genus.

Applicant 's assertions that the nucleic acid of claim 23 is adequately described because it recites a nucleic acid obtained by complementation of yeast nuclear base transport-deficient host cells, specific hybridization conditions, and specific level of identity is incorrect. The nucleic acid of claims 23, part (a), encoding a plant or animal nuclear transporter is described by their activity only. There is known correlation between the structure and function of nuclear transport sequences. In addition, a substantial variation in structures and function is expected among the hybridizing sequences of part (c) because the hybridization conditions as recited in the claim define

low stringency. Also, structural differences also expected among the nucleic acids of part (d) encoding protein with as low as 40% sequence identity to SEQ ID NO: 8 or 9.

Given the broad scope of the claims; the lack of representative number of nucleic acids of the genus claimed; the lack of description for regions in the full-length sequence of SEQ ID NO: 1 that would tolerate modifications or which 10, 50 or 200 bases of SEQ ID NO: 1is capable of antisense inhibition activity; and lack of description in the prior art regarding functional domains essential for base transport activity; the disclosure of few sequences from a single plant species would not provide adequate written description for the genus claimed. Therefore, the rejection is proper.

Claim Rejections - 35 USC § 102/103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 23, 25, 26, 45-46, 57, and 62-63 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Schultes et al (The Plant Cell, vol. 8, pp. 463-475 (1996).

The claims are drawn to an isolated nucleic acid encoding for a plant nuclear base transporter obtained by complementation of yeast nuclear base transporter-deficient host cell. The claims are also drawn to a fragment of said nucleic acid which is at least 10, 50 and 200 nucleotides of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7 or 10, that inhibits the expression of a nuclear base in a host cell when expressed by antisense. The nucleic acid of claim 23 (a) is a product by process.

Schultes et al teach an isolated gene from maize encoding a leaf permease with similarity to pyrimidine and purine transport proteins (see pages 467-468; and Figure 5). The claimed nucleic acid appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. The Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical

comparisons therewith." In re Brown, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). Accordingly the burden shifts to Applicant to provide evidence that the prior art gene would neither anticipate nor render obvious the nucleic acids. See, *MPEP 2113. Also,* the nucleic acid of claims 26 and 45-46 are not expected to possess antisense inhibition activity and are included in the rejection because any prior art gene would contain 10, 50, and 200 nucleotides of the disclosed sequence because the nucleotides need not be contiguous. Absent evidence to the contrary, the rejection is proper.

Claims 23, 25, 26, 28, 30-32, 41, 45-46, 48, 57, and 62 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Abramson et al (US 6, 551, 796, filed 1997).

Abramson et al teach an isolated nucleic acid encoding a human or rat urate transporter (Examples 3 and 11), a construct, plasmid and host cell comprising said nucleic acid operably linked to a promoter functional in a bacterial, mammalian, or yeast cells, and a method of expressing said nucleic acid in said host cells (see at least columns 7-8, columns 13-14, and 18-20). The claimed nucleic acid appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. Accordingly the burden shifts to Applicant to provide evidence that the prior art gene would neither anticipate nor render obvious the nucleic acids. See, *MPEP 2113. Also,* the nucleic acid of claims 26 and 45-46 are not expected to possess antisense inhibition activity and are included in the rejection

because any prior art gene would contain 10, 50, and 200 nucleotides of the disclosed sequence. Absent evidence to the contrary, the rejection is proper.

Conclusion

Claims 29, 33-34, 37-38, 42, 47 are deemed free of the prior art of record.

No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM. Before and after final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

7/5/05
Mai

Medina A. Ibrahim

MEDINA A. IBRAHIM
PATENT EXAMINER